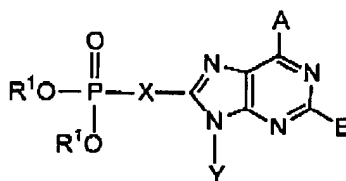


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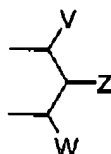
wherein

A is selected from the group consisting of  $-\text{NR}^8$ ,  $-\text{NHSO}_2\text{R}^3$ ,  $-\text{OR}^5$ ,  $-\text{SR}^5$ , halo, lower alkyl,  $-\text{CON}(\text{R}^4)_2$ , guanidino, amidino,  $-\text{H}$ , and perhaloalkyl;

E is selected from the group consisting of  $-\text{H}$ , halo, lower alkylthio, lower perhaloalkyl, lower alkyl, lower alkenyl, lower alkynyl, lower alkoxy,  $-\text{CN}$ , and  $-\text{NR}^7$ ;

X together with Y forms a cyclic group selected from the group of heterocyclic, and aryl;

$\text{R}^1$  is independently selected from the group consisting of  $-\text{H}$ , alkyl, aryl, heteroalicyclic where the cyclic moiety contains a carbonate or thiocarbonate,  $-\text{C}(\text{R}^2)_2\text{-aryl}$ ,  $-\text{alk-aryl}$ ,  $-\text{C}(\text{R}^2)_2\text{OC}(\text{O})\text{NR}^2$ ,  $-\text{NR}^2\text{-C}(\text{O})\text{-R}^3$ ,  $-\text{C}(\text{R}^2)_2\text{-OC}(\text{O})\text{R}^3$ ,  $-\text{C}(\text{R}^2)_2\text{-O-C}(\text{O})\text{OR}^3$ ,  $-\text{C}(\text{R}^2)_2\text{OC}(\text{O})\text{SR}^3$ ,  $-\text{alk-S-C}(\text{O})\text{R}^3$ ,  $-\text{alk-S-S-alkylhydroxy}$ , and  $-\text{alk-S-S-S-alkylhydroxy}$ , or together  $\text{R}^1$  and  $\text{R}^1$  are  $-\text{alk-S-S-alk-}$  to form a cyclic group, wherein each "alk" is an independently selected alkylene, or together  $\text{R}^1$  and  $\text{R}^1$  are



wherein

V and W are independently selected from the group consisting of hydrogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, 1-alkynyl, and  $-\text{R}^9$ ; or

together V and Z are connected via a chain of 3-5 atoms, only one of which can be a heteroatom, to form part of a cyclic group substituted with hydroxy, acyloxy, alkoxy, alkoxy, or aryloxy, or attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus; or

together V and W are connected via a chain of 3 carbon atoms to form part of a cyclic group substituted with hydroxy, acyloxy, alkoxy, alkoxy, alkylthiocarboxy, hydroxymethyl, or aryloxy, or attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus;

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C1  
Z is selected from the group consisting of  $-\text{CH}_2\text{OH}$ ,  $-\text{CH}_2\text{OCOR}^3$ ,  $-\text{CH}_2\text{OC(O)SR}^3$ ,  $-\text{CH}_2\text{OCO}_2\text{R}^3$ ,  $-\text{SR}^3$ ,  $-\text{S(O)R}^3$ ,  $-\text{CH}_2\text{N}_3$ ,  $-\text{CH}_2\text{NR}^2_2$ ,  $-\text{CH}_2\text{Ar}$ ,  $-\text{CH(Ar)OH}$ ,  $-\text{CH}(\text{CH}=\text{CR}^2\text{R}^2)\text{OH}$ ,  $-\text{CH}(\text{C}\equiv\text{CR}^2)\text{OH}$ , and  $-\text{R}^2$ ;

with the provisos that:

- a) V, Z, W are not all -H; and  
b) when Z is  $-\text{R}^2$ , then at least one of V and W is not -H or  $-\text{R}^2$ ;

$\text{R}^2$  is selected from the group consisting of  $\text{R}^3$  and -H;

$\text{R}^3$  is selected from the group consisting of alkyl, aryl, alicyclic, heteroalicyclic, and aralkyl;

$\text{R}^4$  is independently selected from the group consisting of -H, lower alkyl, lower alicyclic, lower heteroalicyclic, lower aralkyl, and lower aryl;

$\text{R}^5$  is selected from the group consisting of lower alkyl, lower aryl, lower aralkyl, lower heteroalicyclic, and lower alicyclic;

$\text{R}^6$  is independently selected from the group consisting of -H, and lower alkyl;

$\text{R}^7$  is independently selected from the group consisting of -H, lower alkyl, lower alicyclic, lower heteroalicyclic, lower aralkyl, lower aryl, and  $-\text{C(O)R}^{10}$ ;

$\text{R}^8$  is independently selected from the group consisting of -H, lower alkyl, lower aralkyl, lower aryl, lower alicyclic,  $-\text{C(O)R}^{10}$ , or together said  $\text{R}^8$  groups form a bidendate alkylene;

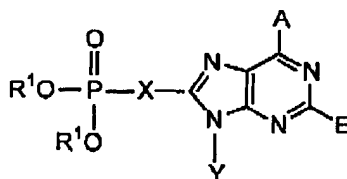
$\text{R}^9$  is selected from the group consisting of alkyl, aralkyl, , heteroalicyclic, and alicyclic;

$\text{R}^{10}$  is selected from the group consisting of -H, lower alkyl,  $-\text{NH}_2$ , lower aryl, and lower perhaloalkyl;

$\text{R}^{11}$  is selected from the group consisting of alkyl, aryl,  $-\text{OH}$ ,  $-\text{NH}_2$  and  $-\text{OR}^3$ ; and pharmaceutically acceptable prodrugs and salts thereof.

C2  
34. (Twice Amended) A method of treating an animal for diabetes mellitus, comprising administering to said animal a therapeutically effective amount of a compound of formula (1):

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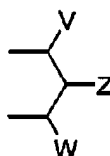
wherein

A is selected from the group consisting of  $-NR^8$ ,  $-NHSO_2R^3$ ,  $-OR^5$ ,  $-SR^5$ , halo, lower alkyl,  $-CON(R^4)_2$ , guanidino, amidino,  $-H$ , and perhaloalkyl;

E is selected from the group consisting of  $-H$ , halo, lower alkylthio, lower perhaloalkyl, lower alkyl, lower alkenyl, lower alkynyl, lower alkoxy,  $-CN$ , and  $-NR^7$ ;

X together with Y forms a cyclic group selected from the group of heterocyclic, and aryl;

$R^1$  is independently selected from the group consisting of  $-H$ , alkyl, aryl, heteroalicyclic where the cyclic moiety contains a carbonate or thiocarbonate,  $-C(R^2)_2$ -aryl,  $-alk-aryl$ ,  $-C(R^2)_2OC(O)NR^2$ ,  $-NR^2-C(O)-R^3$ ,  $-C(R^2)_2-OC(O)R^3$ ,  $-C(R^2)_2-O-C(O)OR^3$ ,  $-C(R^2)_2OC(O)SR^3$ ,  $-alk-S-C(O)R^3$ ,  $-alk-S-S-alkylhydroxy$ , and  $-alk-S-S-S-alkylhydroxy$ , or together  $R^1$  and  $R^1$  are  $-alk-S-S-alk-$  to form a cyclic group, wherein each "alk" is an independently selected alkylene, or together  $R^1$  and  $R^1$  are



wherein

V and W are independently selected from the group consisting of hydrogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, 1-alkynyl, and  $-R^6$ ; or

together V and Z are connected via a chain of 3-5 atoms, only one of which can be a heteroatom, to form part of a cyclic group substituted with hydroxy, acyloxy, alkoxycarboxy, or aryloxycarboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus; or

together V and W are connected via a chain of 3 carbon atoms to form part of a cyclic group substituted with hydroxy, acyloxy, alkoxycarboxy, alkylthiocarboxy, hydroxymethyl, or aryloxycarboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus;

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C2  
Z is selected from the group consisting of  $-\text{CH}_2\text{OH}$ ,  $-\text{CH}_2\text{OCOR}^3$ ,  $-\text{CH}_2\text{OC(O)SR}^3$ ,  $-\text{CH}_2\text{OCO}_2\text{R}^3$ ,  $-\text{SR}^3$ ,  $-\text{S(O)R}^3$ ,  $-\text{CH}_2\text{N}_3$ ,  $-\text{CH}_2\text{NR}^2$ ,  $-\text{CH}_2\text{Ar}$ ,  $-\text{CH(Ar)OH}$ ,  $-\text{CH(CH=CR}^2\text{R}^2)\text{OH}$ ,  $-\text{CH(C=CR}^2\text{R}^2)\text{OH}$ , and  $-\text{R}^2$ ;

with the provisos that:

- a) V, Z, W are not all -H; and  
b) when Z is  $-\text{R}^2$ , then at least one of V and W is not -H or  $-\text{R}^9$ ;

$\text{R}^2$  is selected from the group consisting of  $\text{R}^3$  and -H;

$\text{R}^3$  is selected from the group consisting of alkyl, aryl, alicyclic, heteroalicyclic, and aralkyl;

$\text{R}^4$  is independently selected from the group consisting of -H, lower alkyl, lower alicyclic, lower heteroalicyclic, lower aralkyl, and lower aryl;

$\text{R}^5$  is selected from the group consisting of lower alkyl, lower aryl, lower aralkyl, lower heteroalicyclic, and lower alicyclic;

$\text{R}^6$  is independently selected from the group consisting of -H, and lower alkyl;

$\text{R}^7$  is independently selected from the group consisting of -H, lower alkyl, lower alicyclic, lower heteroalicyclic, lower aralkyl, lower aryl, and  $-\text{C(O)R}^{10}$ ;

$\text{R}^8$  is independently selected from the group consisting of -H, lower alkyl, lower aralkyl, lower aryl, lower alicyclic,  $-\text{C(O)R}^{10}$ , or together said  $\text{R}^8$  groups form a bidendate alkylene;

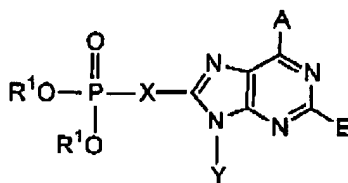
$\text{R}^9$  is selected from the group consisting of alkyl, aralkyl, , heteroalicyclic, and alicyclic;

$\text{R}^{10}$  is selected from the group consisting of -H, lower alkyl,  $-\text{NH}_2$ , lower aryl, and lower perhaloalkyl;

$\text{R}^{11}$  is selected from the group consisting of alkyl, aryl,  $-\text{OH}$ ,  $-\text{NH}_2$  and  $-\text{OR}^3$ ; and pharmaceutically acceptable prodrugs and salts thereof.

35. (Twice Amended) A method of lowering blood glucose levels in an animal in need thereof, comprising administering to said animal a pharmaceutically acceptable amount of a compound of formula (1):

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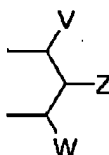
wherein

A is selected from the group consisting of  $-NR^8$ ,  $-NHSO_2R^3$ ,  $-OR^5$ ,  $-SR^5$ , halo, lower alkyl,  $-CON(R^4)_2$ , guanidino, amidino,  $-H$ , and perhaloalkyl;

E is selected from the group consisting of  $-H$ , halo, lower alkylthio, lower perhaloalkyl, lower alkyl, lower alkenyl, lower alkynyl, lower alkoxy,  $-CN$ , and  $-NR^7$ ;

X together with Y forms a cyclic group selected from the group of heterocyclic, and aryl;

$R^1$  is independently selected from the group consisting of  $-H$ , alkyl, aryl, heteroalicyclic where the cyclic moiety contains a carbonate or thiocarbonate,  $-C(R^2)_2$ -aryl,  $-alk-aryl$ ,  $-C(R^2)_2OC(O)NR^2$ ,  $-NR^2-C(O)-R^3$ ,  $-C(R^2)_2-OC(O)R^3$ ,  $-C(R^2)_2-O-C(O)OR^3$ ,  $-C(R^2)_2OC(O)SR^3$ ,  $-alk-S-C(O)R^3$ ,  $-alk-S-S-alkylhydroxy$ , and  $-alk-S-S-S-alkylhydroxy$ , or together  $R^1$  and  $R^1$  are  $-alk-S-S-alk-$  to form a cyclic group, wherein each "alk" is an independently selected alkylene, or together  $R^1$  and  $R^1$  are



wherein

V and W are independently selected from the group consisting of hydrogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, 1-alkynyl, and  $-R^9$ ; or

together V and Z are connected via a chain of 3-5 atoms, only one of which can be a heteroatom, to form part of a cyclic group substituted with hydroxy, acyloxy, alkoxycarboxy, or aryloxycarboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus; or

together V and W are connected via a chain of 3 carbon atoms to form part of a cyclic group substituted with hydroxy, acyloxy, alkoxycarboxy, alkylthiocarboxy, hydroxymethyl, or aryloxycarboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus;

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Z is selected from the group consisting of  $-\text{CH}_2\text{OH}$ ,  $-\text{CH}_2\text{OCOR}^3$ ,  $-\text{CH}_2\text{OC(O)SR}^3$ ,  $-\text{CH}_2\text{OCO}_2\text{R}^3$ ,  $-\text{SR}^3$ ,  $-\text{S(O)R}^3$ ,  $-\text{CH}_2\text{N}_3$ ,  $-\text{CH}_2\text{NR}^2_2$ ,  $-\text{CH}_2\text{Ar}$ ,  $-\text{CH(Ar)OH}$ ,  $-\text{CH}(\text{CH}=\text{CR}^2\text{R}^2)\text{OH}$ ,  $-\text{CH}(\text{C}=\text{CR}^2)\text{OH}$ , and  $-\text{R}^2$ ;

with the provisos that:

- a) V, Z, W are not all  $-\text{H}$ ; and  
b) when Z is  $-\text{R}^2$ , then at least one of V and W is not  $-\text{H}$  or  $-\text{R}^9$ ;

$\text{R}^2$  is selected from the group consisting of  $\text{R}^3$  and  $-\text{H}$ ;

$\text{R}^3$  is selected from the group consisting of alkyl, aryl, alicyclic, heteroalicyclic, and aralkyl;

$\text{R}^4$  is independently selected from the group consisting of  $-\text{H}$ , lower alkyl, lower alicyclic, lower heteroalicyclic, lower aralkyl, and lower aryl;

$\text{R}^5$  is selected from the group consisting of lower alkyl, lower aryl, lower aralkyl, lower heteroalicyclic, and lower alicyclic;

$\text{R}^6$  is independently selected from the group consisting of  $-\text{H}$ , and lower alkyl;

$\text{R}^7$  is independently selected from the group consisting of  $-\text{H}$ , lower alkyl, lower alicyclic, lower heteroalicyclic, lower aralkyl, lower aryl, and  $-\text{C(O)R}^{10}$ ;

$\text{R}^8$  is independently selected from the group consisting of  $-\text{H}$ , lower alkyl, lower aralkyl, lower aryl, lower alicyclic,  $-\text{C(O)R}^{10}$ , or together said  $\text{R}^8$  groups form a bidendate alkylene;

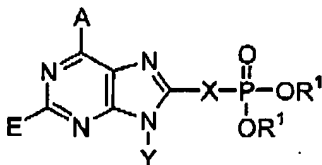
$\text{R}^9$  is selected from the group consisting of alkyl, aralkyl, , heteroalicyclic, and alicyclic;

$\text{R}^{10}$  is selected from the group consisting of  $-\text{H}$ , lower alkyl,  $-\text{NH}_2$ , lower aryl, and lower perhaloalkyl;

$\text{R}^{11}$  is selected from the group consisting of alkyl, aryl,  $-\text{OH}$ ,  $-\text{NH}_2$  and  $-\text{OR}^3$ ; and pharmaceutically acceptable prodrugs and salts thereof.

36. (Twice Amended) A method of inhibiting FBPase at the AMP site in patients in need thereof, comprising administering to said patients an FBPase inhibitory amount of a compound of formula (1):

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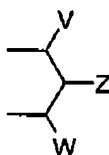
wherein

A is selected from the group consisting of  $-NR^8$ ,  $-NHSO_2R^3$ ,  $-OR^5$ ,  $-SR^5$ , halo, lower alkyl,  $-CON(R^4)_2$ , guanidino, amidino,  $-H$ , and perhaloalkyl;

E is selected from the group consisting of  $-H$ , halo, lower alkylthio, lower perhaloalkyl, lower alkyl, lower alkenyl, lower alkynyl, lower alkoxy,  $-CN$ , and  $-NR^7$ ;

X together with Y forms a cyclic group selected from the group of heterocyclic, and aryl;

$R^1$  is independently selected from the group consisting of  $-H$ , alkyl, aryl, heteroalicyclic where the cyclic moiety contains a carbonate or thiocarbonate,  $-C(R^2)_2$ -aryl,  $-alk$ -aryl,  $-C(R^2)_2OC(O)NR^2$ ,  $-NR^2-C(O)-R^3$ ,  $-C(R^2)_2-OC(O)R^3$ ,  $-C(R^2)_2-O-C(O)OR^3$ ,  $-C(R^2)_2OC(O)SR^3$ ,  $-alk-S-C(O)R^3$ ,  $-alk-S-S-alkylhydroxy$ , and  $-alk-S-S-S-alkylhydroxy$ , or together  $R^1$  and  $R^1$  are  $-alk-S-S-alk-$  to form a cyclic group, wherein each "alk" is an independently selected alkylene, or together  $R^1$  and  $R^1$  are



wherein

V and W are independently selected from the group consisting of hydrogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, 1-alkynyl, and  $-R^9$ ; or

together V and Z are connected via a chain of 3-5 atoms, only one of which can be a heteroatom, to form part of a cyclic group substituted with hydroxy, acyloxy, alkoxy, alkoxy, or aryloxy, attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus;

together V and W are connected via a chain of 3 carbon atoms to form part of a cyclic group substituted with hydroxy, acyloxy, alkoxy, alkoxy, alkylthiocarboxy, hydroxymethyl, or aryloxy, attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus;

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Q2 Z is selected from the group consisting of  $-\text{CH}_2\text{OH}$ ,  $-\text{CH}_2\text{OCOR}^3$ ,  $-\text{CH}_2\text{OC(O)SR}^3$ ,  $-\text{CH}_2\text{OCO}_2\text{R}^3$ ,  $-\text{SR}^3$ ,  $-\text{S(O)R}^3$ ,  $-\text{CH}_2\text{N}_3$ ,  $-\text{CH}_2\text{NR}^2_2$ ,  $-\text{CH}_2\text{Ar}$ ,  $-\text{CH(Ar)OH}$ ,  $-\text{CH}(\text{CH}=\text{CR}^2_2)\text{OH}$ ,  $-\text{CH}(\text{C}=\text{CR}^2_2)\text{OH}$ , and  $-\text{R}^2$ ;

with the provisos that:

- a) V, Z, W are not all  $-\text{H}$ ; and
- b) when Z is  $-\text{R}^2$ , then at least one of V and W is not  $-\text{H}$  or  $-\text{R}^9$ ;

$\text{R}^2$  is selected from the group consisting of  $\text{R}^3$  and  $-\text{H}$ ;

$\text{R}^3$  is selected from the group consisting of alkyl, aryl, alicyclic, heteroalicyclic, and aralkyl;

$\text{R}^4$  is independently selected from the group consisting of  $-\text{H}$ , lower alkyl, lower alicyclic, lower heteroalicyclic, lower aralkyl, and lower aryl;

$\text{R}^5$  is selected from the group consisting of lower alkyl, lower aryl, lower aralkyl, lower heteroalicyclic, and lower alicyclic;

$\text{R}^6$  is independently selected from the group consisting of  $-\text{H}$ , and lower alkyl;

$\text{R}^7$  is independently selected from the group consisting of  $-\text{H}$ , lower alkyl, lower alicyclic, lower heteroalicyclic, lower aralkyl, lower aryl, and  $-\text{C(O)R}^{10}$ ;

$\text{R}^8$  is independently selected from the group consisting of  $-\text{H}$ , lower alkyl, lower aralkyl, lower aryl, lower alicyclic,  $-\text{C(O)R}^{10}$ , or together said  $\text{R}^8$  groups form a bidendate alkylene;

$\text{R}^9$  is selected from the group consisting of alkyl, aralkyl, , heteroalicyclic, and alicyclic;

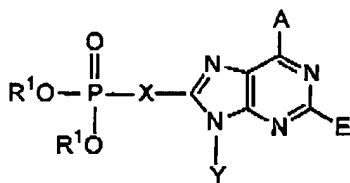
$\text{R}^{10}$  is selected from the group consisting of  $-\text{H}$ , lower alkyl,  $-\text{NH}_2$ , lower aryl, and lower perhaloalkyl;

$\text{R}^{11}$  is selected from the group consisting of alkyl, aryl,  $-\text{OH}$ ,  $-\text{NH}_2$  and  $-\text{OR}^3$ ; and pharmaceutically acceptable prodrugs and salts thereof.

37. (Twice Amended) A method of inhibiting gluconeogenesis in animal in need thereof, comprising administering to said animal an effective amount of a compound of formula (1):



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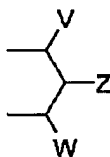
wherein

A is selected from the group consisting of  $-NR^8$ ,  $-NHSO_2R^3$ ,  $-OR^5$ ,  $-SR^5$ , halo, lower alkyl,  $-CON(R^4)_2$ , guanidino, amidino,  $-H$ , and perhaloalkyl;

E is selected from the group consisting of  $-H$ , halo, lower alkylthio, lower perhaloalkyl, lower alkyl, lower alkenyl, lower alkynyl, lower alkoxy,  $-CN$ , and  $-NR^7$ ;

X together with Y forms a cyclic group selected from the group of heterocyclic, and aryl;

$R^1$  is independently selected from the group consisting of  $-H$ , alkyl, aryl, heteroalicyclic where the cyclic moiety contains a carbonate or thiocarbonate,  $-C(R^2)_2$ -aryl,  $-alk$ -aryl,  $-C(R^2)_2OC(O)NR^2$ ,  $-NR^2-C(O)-R^3$ ,  $-C(R^2)_2-OC(O)R^3$ ,  $-C(R^2)_2-O-C(O)OR^3$ ,  $-C(R^2)_2OC(O)SR^3$ ,  $-alk-S-C(O)R^3$ ,  $-alk-S-S-alkylhydroxy$ , and  $-alk-S-S-S-alkylhydroxy$ , or together  $R^1$  and  $R^1$  are  $-alk-S-S-alk-$  to form a cyclic group, wherein each "alk" is an independently selected alkylene, or together  $R^1$  and  $R^1$  are



wherein

V and W are independently selected from the group consisting of hydrogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, 1-alkynyl, and  $-R^9$ ; or

together V and Z are connected via a chain of 3-5 atoms, only one of which can be a heteroatom, to form part of a cyclic group substituted with hydroxy, acyloxy, alkoxycarboxy, or aryloxycarboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus; or

together V and W are connected via a chain of 3 carbon atoms to form part of a cyclic group substituted with hydroxy, acyloxy, alkoxycarboxy, alkylthiocarboxy, hydroxymethyl, or aryloxycarboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus;

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Z is selected from the group consisting of  $-\text{CH}_2\text{OH}$ ,  $-\text{CH}_2\text{OCOR}^3$ ,  $-\text{CH}_2\text{OC(O)SR}^3$ ,  $-\text{CH}_2\text{OCO}_2\text{R}^3$ ,  $-\text{SR}^3$ ,  $-\text{S(O)R}^3$ ,  $-\text{CH}_2\text{N}_3$ ,  $-\text{CH}_2\text{NR}^2_2$ ,  $-\text{CH}_2\text{Ar}$ ,  $-\text{CH(Ar)OH}$ ,  $-\text{CH}(\text{CH}=\text{CR}^2\text{R}^2)\text{OH}$ ,  $-\text{CH}(\text{C}=\text{CR}^2)\text{OH}$ , and  $-\text{R}^2$ ;

with the provisos that:

- a) V, Z, W are not all  $-\text{H}$ ; and  
b) when Z is  $-\text{R}^2$ , then at least one of V and W is not  $-\text{H}$  or  $-\text{R}^9$ ;

$\text{R}^2$  is selected from the group consisting of  $\text{R}^3$  and  $-\text{H}$ ;

$\text{R}^3$  is selected from the group consisting of alkyl, aryl, alicyclic, heteroalicyclic, and aralkyl;

$\text{R}^4$  is independently selected from the group consisting of  $-\text{H}$ , lower alkyl, lower alicyclic, lower heteroalicyclic, lower aralkyl, and lower aryl;

$\text{R}^5$  is selected from the group consisting of lower alkyl, lower aryl, lower aralkyl, lower heteroalicyclic, and lower alicyclic;

$\text{R}^6$  is independently selected from the group consisting of  $-\text{H}$ , and lower alkyl;

$\text{R}^7$  is independently selected from the group consisting of  $-\text{H}$ , lower alkyl, lower alicyclic, lower heteroalicyclic, lower aralkyl, lower aryl, and  $-\text{C(O)R}^{10}$ ;

$\text{R}^8$  is independently selected from the group consisting of  $-\text{H}$ , lower alkyl, lower aralkyl, lower aryl, lower alicyclic,  $-\text{C(O)R}^{10}$ , or together said  $\text{R}^8$  groups form a bidendate alkylene;

$\text{R}^9$  is selected from the group consisting of alkyl, aralkyl, , heteroalicyclic, and alicyclic;

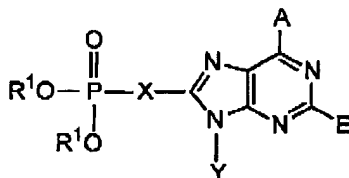
$\text{R}^{10}$  is selected from the group consisting of  $-\text{H}$ , lower alkyl,  $-\text{NH}_2$ , lower aryl, and lower perhaloalkyl;

$\text{R}^{11}$  is selected from the group consisting of alkyl, aryl,  $-\text{OH}$ ,  $-\text{NH}_2$  and  $-\text{OR}^3$ ; and pharmaceutically acceptable prodrugs and salts thereof.

39. (Twice Amended) A method of treating an animal for a disease derived from abnormally elevated insulin levels, comprising administering to said animal a therapeutically

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effective amount of a fructose-1,6-bisphosphatase inhibitor wherein said inhibitor is a compound of formula (1):



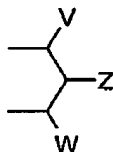
wherein

A is selected from the group consisting of  $-NR^8$ ,  $-NHSO_2R^3$ ,  $-OR^5$ ,  $-SR^5$ , halo, lower alkyl,  $-CON(R^6)_2$ , guanidino, amidino,  $-H$ , and perhaloalkyl;

E is selected from the group consisting of  $-H$ , halo, lower alkylthio, lower perhaloalkyl, lower alkyl, lower alkenyl, lower alkynyl, lower alkoxy,  $-CN$ , and  $-NR^7$ ;

X together with Y forms a cyclic group selected from the group of heterocyclic, and aryl;

$R^1$  is independently selected from the group consisting of  $-H$ , alkyl, aryl, heteroalicyclic where the cyclic moiety contains a carbonate or thiocarbonate,  $-C(R^2)_2$ -aryl,  $-alk-aryl$ ,  $-C(R^2)_2OC(O)NR^2$ ,  $-NR^2-C(O)-R^3$ ,  $-C(R^2)_2-OC(O)R^3$ ,  $-C(R^2)_2-O-C(O)OR^3$ ,  $-C(R^2)_2OC(O)SR^3$ ,  $-alk-S-C(O)R^3$ ,  $-alk-S-S-alkylhydroxy$ , and  $-alk-S-S-S-alkylhydroxy$ , or together  $R^1$  and  $R^1$  are  $-alk-S-S-alk-$  to form a cyclic group, wherein each "alk" is an independently selected alkylene, or together  $R^1$  and  $R^1$  are



wherein

V and W are independently selected from the group consisting of hydrogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, 1-alkynyl, and  $-R^9$ ; or

together V and Z are connected via a chain of 3-5 atoms, only one of which can be a heteroatom, to form part of a cyclic group substituted with hydroxy, acyloxy, alkoxycarboxy, or aryloxycarboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus; or

together V and W are connected via a chain of 3 carbon atoms to form part of a cyclic group substituted with hydroxy, acyloxy, alkoxycarboxy, alkylthiocarboxy,

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hydroxymethyl, or aryloxycarboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus;

C-3 Z is selected from the group consisting of  $-\text{CH}_2\text{OH}$ ,  $-\text{CH}_2\text{OCOR}^3$ ,  $-\text{CH}_2\text{OC}(\text{O})\text{SR}^3$ ,  $-\text{CH}_2\text{OCO}_2\text{R}^3$ ,  $-\text{SR}^3$ ,  $-\text{S}(\text{O})\text{R}^3$ ,  $-\text{CH}_2\text{N}_3$ ,  $-\text{CH}_2\text{NR}^2$ ,  $-\text{CH}_2\text{Ar}$ ,  $-\text{CH}(\text{Ar})\text{OH}$ ,  $-\text{CH}(\text{CH}=\text{CR}^2\text{R}^2)\text{OH}$ ,  $-\text{CH}(\text{C}\equiv\text{CR}^2)\text{OH}$ , and  $-\text{R}^2$ ;

with the provisos that:

- a) V, Z, W are not all  $-\text{H}$ ; and
- b) when Z is  $-\text{R}^2$ , then at least one of V and W is not  $-\text{H}$  or  $-\text{R}^9$ ;

$\text{R}^2$  is selected from the group consisting of  $\text{R}^3$  and  $-\text{H}$ ;

$\text{R}^3$  is selected from the group consisting of alkyl, aryl, alicyclic, heteroalicyclic, and aralkyl;

$\text{R}^4$  is independently selected from the group consisting of  $-\text{H}$ , lower alkyl, lower alicyclic, lower heteroalicyclic, lower aralkyl, and lower aryl;

$\text{R}^5$  is selected from the group consisting of lower alkyl, lower aryl, lower aralkyl, lower heteroalicyclic, and lower alicyclic;

$\text{R}^6$  is independently selected from the group consisting of  $-\text{H}$ , and lower alkyl;

$\text{R}^7$  is independently selected from the group consisting of  $-\text{H}$ , lower alkyl, lower alicyclic, lower heteroalicyclic, lower aralkyl, lower aryl, and  $-\text{C}(\text{O})\text{R}^{10}$ ;

$\text{R}^8$  is independently selected from the group consisting of  $-\text{H}$ , lower alkyl, lower aralkyl, lower aryl, lower alicyclic,  $-\text{C}(\text{O})\text{R}^{10}$ , or together said  $\text{R}^8$  groups form a bidendate alkylene;

$\text{R}^9$  is selected from the group consisting of alkyl, aralkyl, , heteroalicyclic, and alicyclic;

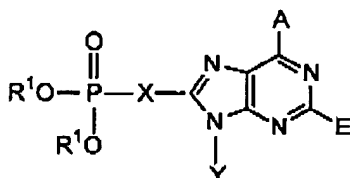
$\text{R}^{10}$  is selected from the group consisting of  $-\text{H}$ , lower alkyl,  $-\text{NH}_2$ , lower aryl, and lower perhaloalkyl;

$\text{R}^{11}$  is selected from the group consisting of alkyl, aryl,  $-\text{OH}$ ,  $-\text{NH}_2$  and  $-\text{OR}^3$ ; and pharmaceutically acceptable prodrugs and salts thereof.

C4 42. (Twice Amended) A method of treating an animal with excess glycogen storage disease, comprising administering to said animal in need thereof a therapeutically

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C4  
effective amount of a fructose-1,6-bisphosphatase inhibitor, wherein said inhibitor is a compound of formula (1):



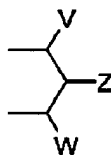
wherein

A is selected from the group consisting of  $-\text{NR}^8_2$ ,  $-\text{NHSO}_2\text{R}^3$ ,  $-\text{OR}^5$ ,  $-\text{SR}^5$ , halo, lower alkyl,  $-\text{CON}(\text{R}^4)_2$ , guanidino, amidino,  $-\text{H}$ , and perhaloalkyl;

E is selected from the group consisting of  $-\text{H}$ , halo, lower alkylthio, lower perhaloalkyl, lower alkyl, lower alkenyl, lower alkynyl, lower alkoxy,  $-\text{CN}$ , and  $-\text{NR}^7_2$ ;

X together with Y forms a cyclic group selected from the group of heterocyclic, and aryl;

$\text{R}^1$  is independently selected from the group consisting of  $-\text{H}$ , alkyl, aryl, heteroalicyclic where the cyclic moiety contains a carbonate or thiocarbonate,  $-\text{C}(\text{R}^2)_2\text{-aryl}$ ,  $-\text{alk-aryl}$ ,  $-\text{C}(\text{R}^2)_2\text{OC}(\text{O})\text{NR}^2_2$ ,  $-\text{NR}^2\text{-C}(\text{O})\text{-R}^3$ ,  $-\text{C}(\text{R}^2)_2\text{-OC}(\text{O})\text{R}^3$ ,  $-\text{C}(\text{R}^2)_2\text{-O-C}(\text{O})\text{OR}^3$ ,  $-\text{C}(\text{R}^2)_2\text{OC}(\text{O})\text{SR}^3$ ,  $-\text{alk-S-C}(\text{O})\text{R}^3$ ,  $-\text{alk-S-S-alkylhydroxy}$ , and  $-\text{alk-S-S-S-alkylhydroxy}$ , or together  $\text{R}^1$  and  $\text{R}^1$  are  $-\text{alk-S-S-alk-}$  to form a cyclic group, wherein each "alk" is an independently selected alkylene, or together  $\text{R}^1$  and  $\text{R}^1$  are



wherein

V and W are independently selected from the group consisting of hydrogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, 1-alkynyl, and  $-\text{R}^9$ ; or

together V and Z are connected via a chain of 3-5 atoms, only one of which can be a heteroatom, to form part of a cyclic group substituted with hydroxy, acyloxy, alkoxycarboxy, or aryloxycarboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus; or

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together V and W are connected via a chain of 3 carbon atoms to form part of a cyclic group substituted with hydroxy, acyloxy, alkoxycarboxy, alkylthiocarboxy, hydroxymethyl, or aryloxycarboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus;

Z is selected from the group consisting of  $-\text{CH}_2\text{OH}$ ,  $-\text{CH}_2\text{OCOR}^3$ ,  $-\text{CH}_2\text{OC(O)SR}^3$ ,  $-\text{CH}_2\text{OCO}_2\text{R}^3$ ,  $-\text{SR}^3$ ,  $-\text{S(O)R}^3$ ,  $-\text{CH}_2\text{N}_3$ ,  $-\text{CH}_2\text{NR}^2_2$ ,  $-\text{CH}_2\text{Ar}$ ,  $-\text{CH(Ar)OH}$ ,  $-\text{CH}(\text{CH}=\text{CR}^2\text{R}^2)\text{OH}$ ,  $-\text{CH}(\text{C}\equiv\text{CR}^2)\text{OH}$ , and  $-\text{R}^2$ ;

with the provisos that:

- a)  $V, Z, W$  are not all  $-H$ ; and
- b) when  $Z$  is  $-R^2$ , then at least one of  $V$  and  $W$  is not  $-H$  or  $-R^9$ ;

$R^2$  is selected from the group consisting of  $R^3$  and  $-H$ ;

$R^3$  is selected from the group consisting of alkyl, aryl, alicyclic, heteroalicyclic, and aralkyl;

$R^4$  is independently selected from the group consisting of -H, lower alkyl, lower alicyclic, lower heteroalicyclic, lower aralkyl, and lower aryl;

**R<sup>5</sup> is selected from the group consisting of lower alkyl, lower aryl, lower aralkyl, lower heteroalicyclic, and lower alicyclic;**

**R<sup>6</sup> is independently selected from the group consisting of -H, and lower alkyl;**

$R^7$  is independently selected from the group consisting of -H, lower alkyl, lower alicyclic, lower heteroalicyclic, lower aralkyl, lower aryl, and  $-C(O)R^{10}$ ;

$R^8$  is independently selected from the group consisting of -H, lower alkyl, lower aralkyl, lower aryl, lower alicyclic,  $-C(O)R^{10}$ , or together said  $R^8$  groups form a bidentate alkylene;

R<sup>9</sup> is selected from the group consisting of alkyl, aralkyl, , heteroalicyclic, and alicyclic;

$R^{10}$  is selected from the group consisting of -H, lower alkyl, -NH<sub>2</sub>, lower aryl, and lower perhaloalkyl;

R<sup>11</sup> is selected from the group consisting of alkyl, aryl, -OH, -NH<sub>2</sub> and -OR<sup>3</sup>; and pharmaceutically acceptable prodrugs and salts thereof.